IN THE ABSTRACT OF THE DISCLOSURE

Please add the abstract of the disclosure on a separate sheet.

REMARKS

This amendment is submitted in an earnest effort to advance the prosecution of this application.

Applicants have amended the title of this application per the Examiner's suggestion.

Applicants note that the drawing in this application is informal. In the event that allowable subject matter is found Applicants will submit new formal drawings in full compliance with the Rules of Practice.

Applicants are submitting herewith certified copies of German Patent Applications 197 43 894.6 filed 4 October 1997 and 198 31 609.7 filed 14 July 1998 together with English translations of thereof.

Applicants are including a new sequence listing that includes SEQ ID NO: 1, 2, 3 and 4. SEQ ID NOS: 1 and 2 are the same sequences as previously presented and are respectively the polynucleotide that includes the pyruvate carboxylase gene isolated from C. glutamicum and the enzyme expressed by the pyruvate carboxylase gene. SEQ ID. NOS: 3 and 4 have antecedent basis on page 10 of the application and are PCR primers used in the cloning of the polynucleotide that is SEQ ID NO:1. A computer-readable disk is also included with the sequence information. Also included are

statements signed by the undersigned attorney of record under 37 CFR 1.821(f) that the information on the computer-readable disk and the information on the written sequence listing is the same and under 37 CFR 1.821(g) that in the preparation of the sequence listings no new matter has been inserted into the application.

Applicants are submitting a substitute specification that includes correction of the minor informalities pointed out by the Examiner. The substitute specification includes a Brief Descriptions of the Drawings, namely Figures 1 and 2. The substitute specification is accompanied by a marked-up version of the original specification. In the opinion of the undersigned attorney of record the substitute specification includes no inserted prohibited new matter.

Applicants have cancelled claims 1 through 17 and 32 through 51 and are replacing those claims with claims 52 through 69. Antecedent basis for claims 52 through 65 may be found in the original specification on pages 5 through 9.

Applicants note that the Examiner has maintained his requirement for restriction and has cited a new reference: Morris et al, Biochem. Biophys. Res. Commun. 145: 390-6 in support of his argument that restriction is proper. It is noted that the Examiner has withdrawn all claims beyond the scope of the elected claims of Group II from further consideration. Applicants have cancelled claims 1 through 17 and 32 through 37 directed to the non-elected claims of Groups I and III. However, Applicants have added claims 66 through 69 to replace the cancelled claims of original Group I.

Claims 66 through 69 concentrate on the pyruvate carboxylase gene that expresses an amino acid of SEQ ID NO: 2 and on the pyruvate carboxylase gene having SEQ ID NO:1. It is the structure of this amino acid sequence and this gene sequence that is the common technical feature between claims 66 through 69 and the claims falling within the scope of Group II. Applicants ask that the Examiner consider claims 66 through 69 in conjunction with the claims of Group II, that is claims 52 through 65 now presented.

There is no disclosure or suggestion in the Morris et al reference of an isolated pyruvate carboxylase gene having SEQ ID NO:1 or an amino acid sequence having SEQ ID NO:2. MORRIS et al discloses a sequence for a pyruvate carboxylase gene obtained from Saccharomyces cerevisiae that is structurally far removed from the pyruvate carboxylase of SEQ ID NO:1. While there are some conserved regions between the two pyruvate carboxylase genes, the genes are certainly nowhere near 100% homologous. See page 9, lines 10 through 17 and page 13 of the original English specification.

The Examiner has rejected claims 39 through 45, 48, 50 and 51 last presented under 35 USC 112, second paragraph, as indefinite. Applicants have cancelled claims 39 through 51 and are submitting new claims 52 through 69 which are believed to be in full compliance with the requirements of the statute. Applicants have responded to Paragraph 9 of the office action by submitting claims which do not use the term "a substantially identically effective DNA sequence.' Instead claims 52 through 69 concentrate

on the structure of the isolated pyruvate carboxylase gene of SEQ ID NO:1 or on allele variations thereof as well as on the structure of the amino acid sequence of SEQ ID NO:2 or on amino acid sequences expressed by an allele variation of the pyruvate carboxylase gene coding for the amino acid sequence given under SEQ ID NO:2 wherein the allele variation is a deletion, insertion, or substitution of a nucleotide in said isolated pyruvate carboxylase gene coding for the amino acid sequence given under SEQ ID NO:2.

In response to Paragraph 10 of the office action Applicants have presented claims which include proper antecedent basis for terms such as -- a regulatory sequence -- as in claim 56.

None of the claims now presented uses the language that the Examiner has found indefinite according to Paragraph 11 of the office action.

Applicants have followed the suggestions set forth by the Examiner in Paragraph 12 of the office action. See new claims 58 and 62 which replace claims 44 and 48.

Claims 50 and 51 have been cancelled without replacement so the rejection of these claims set forth in Paragraph 12 has become moot.

The Examiner has rejected claims 38 through 51 last presented under 35 USC 112, first paragraph as based upon a specification that both fails to describe the invention as broadly claimed and to enable one "skilled in the art" to make or to use the invention commensurate in scope with the claims. Applicants have cancelled these claims and are submitting new claims 52

through 69 which are believed to be in full compliance with the statute.

Applicants do not agree that in order to comply with the requirements of 35 USC 112, first paragraph, Applicants must put the public into possession of the attributes and features of all species within the claimed genus. Applicants do not have to pinpoint where each allele variation in the pyruvate carboxylase gene of SEQ ID NO: 1 is located. Applicants have defined the allele variation as a deletion, insertion, or substitution of a nucleotide in said isolated pyruvate carboxylase gene. These variations in terms of the particular nucleotide in a particular location in the gene structure may be known in the art at the present time or may be determined in the future. In any event such a definition of the polynucleotide as a pyruvate carboxylase gene of SEQ ID NO: 1 or an allele variation thereof that merely is a deletion, insertion, or substitution of a nucleotide in said isolated pyruvate carboxylase gene is a narrow, sufficiently specific definition of the polynucleotide that is adequately supported by the present application in terms of both description of the invention and enablement.

Point mutations including insertions, deletions and substitutions are well known natural occurrences in the structure of genes. In fact cols. 6 and 7 of U.S. Patent 6,171,833 states that part of the invention disclosed therein includes variants on the gene structure that corresponds to the instant SEQ ID NO:1 in the present application and that these variants include substitu-

tions, deletions or additions. Applicants contend that these point mutations are a common natural occurrence in isolated genes and one "skilled in the art" would expect that from time to time an allele variation in a naturally occurring gene sequence with over 3700 base pairs will occur. Often these variants will express the same amino acid sequence or a similar amino acid sequence with the same enzymatic activity. However, even if the allele variation results in substantial loss of the enzymatic activity of the expressed product, the allele variation would still have use as a gene probe. See col. 7, lines 8 through 17 of U.S. Patent 6,171,833. Under these circumstances why should Applicants be limited to only the gene sequence of SEQ ID NO:1 and receive no protection for variants with only an insertion, deletion or substitution of a nucleotide? One "skilled in the art" would be able to recognize gene sequences identical to that of SEQ ID NO:1 but with an insertion, deletion or substitution and would be able to employ such gene sequences the same way that the gene sequence of SEQ ID NO:1 is employed without the need to conduct undue experimentation. If the variant gene sequence expresses an enzyme with little or know activity relative to the pyruvate carboxylase of SEQ ID NO:2, all that the "skilled worker need do is to abandon using the variant sequence. Or as suggested in col. 7, lines 8 through 17 even when a particular gene sequence does not express a polypeptide with enzymatic activity, one "skilled in the art" would still know how to use the corresponding polynucleotide as a genetic probe. Thus claims 52, 53 and the claims dependent upon claim 52 as well as claims 66 and 68 are

supported and enabled by the disclosure in the specification and none of these claims should be rejected under 35 USC 112.

Applicants also believe that claims 60 to 63 directed to a transformed cell are adequately supported by the specification. in the present application only two species of "transformed cells" are disclosed. First of all in Example 3 (page 14, line 26) the isolated nucleotide sequence is transformed into the corynebacterium glutamicum wild type ATCC 13032 and the corresponding overexpression of the pyruvate-carboxylase is measured. Further the transfer of the nucleotide sequence into C. glutamicum strain DG 52-5 is described in Example 4. Example 5 discloses the transformation of the strain C. glutamicum DM 368-3. In addition page 6, line 26 to page 7, line 2 of the specification discloses that the transformation of the nucleotide sequence of the invention can generally be transferred in microorganisms suited for the production of amino acid. Particularly suited are gram-positive bacteria, such as the representatives of enterobacteria, and here particularly E. coli or Serratia.

Applicants further point out that through Example 3, wherein the corynebacterium wild type was transformed, it is clear to the person skilled in the art that also all deletions of this wild type, such as targeted optimized production strains, or also strains obtained through untargeted, chemical mutagenesis of the species corynebacterium are suited for improved amino acid production through transformation with the sequence of the invention. This way the person skilled in the art is offered a multitude of

Examples for organisms which are suited for the transformation and overexpression of the nucleotide sequence of the invention and for improvement of the amino acid production based on this transformation. Furthermore the present invention is so clearly disclosed that a person skilled in the art can reproduce it without further ado. The various embodiment examples support that with concrete data. It is therefor also clearly shown that the inventors were in possession of the present invention. Therefore no rejection of any of claims 60 to 63 should be maintained under 35 USC 112, first paragraph as beyond the scope of the enabling disclosure.

Applicants specifically point to claims 64, 65, 67 and 69 which are narrower claims that relate directly to the pyruvate carboxylase gene of SEQ ID NO:1 or to an amino acid sequence of SEQ ID NO:2 that is expressed by the pyruvate carboxylase gene of SEQ ID NO:1. Thus even if the Examiner does not agree that the remaining claims in this case are in condition for allowance, there should be no doubt that these narrow claims cover allowable subject matter and that interference with U.S. Patent 6,171,833 can proceed.

The Examiner has rejected claims 38 through 51 under 35 USC 102 as anticipated by either PETERS-WENDISCH et al (AT) or KOFFAS et al. Applicants believe that neither of these references is an effective reference in this application because Applicants have the right to rely on the priority of their German Patent Applications 197 43 894.6 filed 4 October 1997 and 198 31 609.7 filed 14 July 1998. As can be seen from the certified English

translation of German Patent Applications 197 43 894.6 there is support for all four polynucleotide sequences, SEQ ID NO: 1,2, 3 and 4. The same example as in the present application is set forth on pages 10 through 19 of the English translation except that Table 4 is not included. Figures 1 and 2 are also included in German Patent Applications 197 43 894.6. It is only the data in Table 4 that is present in both the instant application and in German Patent Application 198 31 609.7 filed 14 July 1998 that is not found in the original German priority document. In any event Applicants have every right to rely on the support provided by German Patent Applications 197 43 894.6 to establish a date of invention pursuant to the International Convention of 4 October 1997.

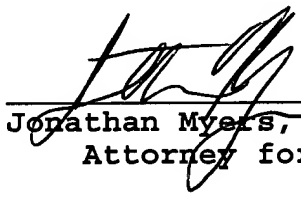
The publication dates of Peters-Wendisch et al, Microbiology 144:915 to 927 (1998), "Pyruvate Carboxylase from Corynebacterium Glutamicum" and of Koffas et al, Appl. Microbiol. Biotechnol. (1998) 50: 346 to 352, "Sequence of the Corynebacterium glutamicum pyruvate carboxylase gene" are both 1998 dates subsequent to the priority date of German Patent Applications 197 43 894.6. In fact the KOFFAS et al reference was not published until 24 September 1998. Now that Applicants have made of record certified copies of their priority documents and certified English translations thereof, neither of these references is an effective reference in this case.

Accordingly none of the bases for rejection of any claim in this case as either anticipated by Peters-Wendisch et al or

Koffas et al or as obvious in view of Peters-Wendisch et al or Koffas et al or as obvious in view of these two references in combination or in further combination with de Boer et al should be maintained.

Favorable action in this case is earnestly solicited. Applicants are enclosing a petition to obtain a one month extension of the term for response and authorization to pay the extension fee by credit card.

Respectfully submitted,
The Firm of Karl F. Ross P.C.



Jonathan Myers, Reg. No. 26,963
Attorney for Applicant

er
28 January 2002
5676 Riverdale Avenue Box 900
Bronx, NY 10471-0900
Cust. No.: 535
Tel: (718) 884-6600
Fax: (718) 601-1099

Enclosures: Two certified German priority documents
Two certified English translation
Substitute specification
Marked up copy of original specification
Hard copy of sequence data
Computer readable Disk of sequence data
Petition for one month extension